AMENDMENTS TO THE CLAIMS:

This listing of claims replaces all prior versions and listings of claims in the application:

Listing of Claims:

1. (Currently amended) A computer implemented method for predicting the structure of a membrane-bound protein having a plurality of [[α-]]helical regions, comprising:

providing an amino acid sequence for the membrane-bound protein;

~~using the amino acid sequence to~~ identifying ~~one~~ two or more ranges of amino acids in the amino acid sequence as transmembrane regions of the membrane-bound protein;

constructing each of two or more helices in a set of helices for the transmembrane regions;

~~and~~ optimizing a helix bundle configuration for the set of helices using a first molecular dynamics simulation;

after optimizing the helix bundle configuration, constructing one or more ~~a plurality of~~ inter-helical loops to generate a full-atom model of the membrane-bound protein;

optimizing the full-atom model using a second molecular dynamics simulation; and

outputting a predicted structure for the ~~transmembrane~~-bound protein based on the second optimization.

2. (Withdrawn) A computational model of the structure of a transmembrane protein having a plurality of α-helical regions, the computational model comprising:

a computer-readable memory storing data describing an optimized predicted three-dimensional structure for the transmembrane protein, the optimized predicted structure being generated according to the method of claim 1.

3. (Currently amended) The method of claim 1, wherein:

constructing each of two or more helices in the set of helices for the transmembrane regions includes constructing each of two or more ~~a set of~~ canonical helices corresponding to the transmembrane regions, calculating a minimum-energy configuration for each of the canonical helices, and optimizing each of the canonical helices~~, assembling a helix bundle including each of the set of helices, and calculating a minimum-energy configuration for the helix bundle in a lipid bilayer.~~

4. (Withdrawn) A computational method for modeling the structure of a transmembrane protein having a plurality of α-helical regions, the method comprising:

providing amino acid sequence information and sequence alignment information for a transmembrane protein having a plurality of α-helical regions;

using the amino acid sequence information and the sequence alignment information to predict a set of transmembrane segments of the transmembrane protein;

constructing canonical helices for the predicted transmembrane segments and optimizing the canonical helices using a first molecular dynamics simulation;

combining the optimized helices based on the sequence alignment information to form a helix bundle, and assembling the helix bundle with a lipid bilayer to form a system helix bundle;

optimizing the structure of the system helix bundle using a second molecular dynamics simulation;

adding inter-helical loops to the system helix bundle to form a full atom model;

optimizing the full atom model using a third molecular dynamics simulation; and

outputting a predicted structure for the transmembrane protein based on the third optimization.

5. (Withdrawn) The method of claim 4, wherein:

the transmembrane protein is a G-protein coupled receptor.

6. (Withdrawn) The method of claim 4, wherein:

an energy minimum is calculated for each of the canonical helices before forming the helix bundle.

7. (Withdrawn) The method of claim 4, further comprising:

determining the periodicity of hydrophobic residues identified in the amino acid sequence information; and

identifying a plurality of lipid-accessible residues based at least in part on the identified periodicity.

8. (Withdrawn) The method of claim 4, wherein:

combining the helices based on the sequence information to form a helix bundle includes orienting the helix axes according to the 7.5 Å electron density map for rhodopsin.

9. (Withdrawn) The method of claim 7, wherein:

combining the helices based on the sequence information to form a helix bundle includes orienting the identified lipid-accessible residues to face the outside of the helix bundle.

10. (Withdrawn) The method of claim 4, wherein:

the first molecular dynamics simulation is a torsional molecular dynamics simulation.

11. (Withdrawn) The method of claim 4, wherein:

the second molecular dynamics simulation is a rigid body molecular dynamics simulation.

12. (Withdrawn) The method of claim 11, wherein:

the first molecular dynamics simulation is a Newton-Euler Inverse Mass Operator dynamics simulation.

13. (Withdrawn) The method of claim 4, wherein:

the third molecular dynamics simulation is a mixed mode molecular dynamics simulation.

14. (Withdrawn) The method of claim 4, wherein:
at least the third molecular dynamics simulation includes a solvent approximation.

15. (Withdrawn) The method of claim 14, wherein:
the solvent approximation is a continuum solvation model.

16. (Withdrawn) The method of claim 15, wherein:
the solvent approximation includes the Surface Generalized Born model.

17. (Withdrawn) The method of claim 15, wherein:
the solvent approximation includes the Poisson-Boltzmann description.

18. (Withdrawn) The method of claim 14, wherein:
the solvent approximation is an empirical approximation comprising estimating solvation free energy as a function of solvent accessible protein surface area.

19. (Withdrawn) The method of claim 4, wherein:
the predicted structure is generated by performing the third molecular dynamics simulation for a time in the range from about 100ps to about 1 ns.

20. (Withdrawn) A computational model of the structure of a transmembrane protein having a plurality of α-helical regions, the computational model comprising:
a computer-readable data storage medium storing data describing an optimized predicted three-dimensional structure for the transmembrane protein, the optimized predicted structure being generated according to the method of claim 4.

21. (Withdrawn) The computational model of claim 20, wherein: the transmembrane protein is olfactory receptor S6.

22. (Withdrawn) The computational model of claim 20, wherein: the transmembrane protein is olfactory receptor S18.

23. (Withdrawn) The computational model of claim 20, wherein: the transmembrane protein is olfactory receptor S19.

24. (Withdrawn) The computational model of claim 20, wherein: the transmembrane protein is olfactory receptor S25.

25. (Withdrawn) The computational model of claim 20, wherein: the transmembrane protein is olfactory receptor S46.

26. (Withdrawn) The computational model of claim 20, wherein: the transmembrane protein is olfactory receptor S50.

27. (Withdrawn) A computer program product on a computer-readable medium for predicting the structure of a membrane-bound protein having a plurality of α-helical regions, the computer program product comprising instructions operable to cause a programmable processor to:

provide an amino acid sequence for the membrane-bound protein;

use the amino acid sequence to identify one or more transmembrane regions of the membrane-bound protein;

construct a set of helices for the transmembrane regions and optimize a helix bundle configuration for the set of helices using a first molecular dynamics simulation;

construct a plurality of inter-helical loops to generate a full-atom model of the membrane-bound protein;

optimize the full-atom model using a second molecular dynamics simulation;

output a predicted structure for the transmembrane protein based on the second optimization.

28. (Withdrawn) A computer program product on a computer-readable medium for predicting the structure of a G-protein coupled receptor having a plurality of α-helical regions, the computer program product comprising instructions operable to cause a programmable processor to:

provide amino acid sequence information and sequence alignment information for a G-protein coupled receptor;

use the amino acid sequence information and the sequence alignment information to predict a set of transmembrane segments of the G-protein coupled receptor;

construct canonical helices for the predicted transmembrane segments and optimize the canonical helices using a first molecular dynamics simulation;

combine the optimized helices based on the sequence alignment information to form a helix bundle and assemble the helix bundle with a lipid bilayer to form a system helix bundle;

optimize the structure of the system helix bundle using a second molecular dynamics simulation;

add inter-helical loops to the system helix bundle to form a full atom model;

optimize the full atom model using a third molecular dynamics simulation; and

output a predicted structure for the G-protein coupled receptor based on the second optimization.

29. (Withdrawn) A computational model of the structure of a G-protein coupled receptor, the computational model comprising:

a computer-readable data storage medium storing data describing a three-dimensional structure for olfactory receptor S6, the data describing the predicted structure including structure coordinates for the amino acids of olfactory receptor S6 having a root mean square deviation from the structure coordinates of the backbone atoms of the amino acids as set out in Table 2 of less than or equal to about 2.0 angstroms.

30. (Withdrawn) A computational model of the structure of a G-protein coupled receptor, the computational model comprising:

a computer-readable data storage medium storing data describing a three-dimensional structure for olfactory receptor S18, the data describing the predicted structure including structure coordinates for the amino acids of olfactory receptor S18 having a root mean square deviation from the structure coordinates of the backbone atoms of the amino acids as set out in Table 3 of less than or equal to about 2.0 angstroms.

31. (Withdrawn) A computational model of the structure of a G-protein coupled receptor, the computational model comprising:

a computer-readable data storage medium storing data describing a three-dimensional structure for olfactory receptor S19, the data describing the predicted structure including structure coordinates for the amino acids of olfactory receptor S19 having a root mean square deviation from the structure coordinates of the backbone atoms of the amino acids as set out in Table 4 of less than or equal to about 2.0 angstroms.

32. (Withdrawn) A computational model of the structure of a G-protein coupled receptor, the computational model comprising:

a computer-readable data storage medium storing data describing a three-dimensional structure for olfactory receptor S25, the data describing the predicted structure including structure coordinates for the amino acids of olfactory receptor S25 having a root mean square

deviation from the structure coordinates of the backbone atoms of the amino acids as set out in Table 5 of less than or equal to about 2.0 angstroms.

33. (Withdrawn) A computational model of the structure of a G-protein coupled receptor, the computational model comprising:

a computer-readable data storage medium storing data describing a three-dimensional structure for olfactory receptor S46, the data describing the predicted structure including structure coordinates for the amino acids of olfactory receptor S46 having a root mean square deviation from the structure coordinates of the backbone atoms of the amino acids as set out in Table 6 of less than or equal to about 2.0 angstroms.

34. (Withdrawn) A computational model of the structure of a G-protein coupled receptor, the computational model comprising:

a computer-readable data storage medium storing data describing a three-dimensional structure for olfactory receptor S50, the data describing the predicted structure including structure coordinates for the amino acids of olfactory receptor S50 having a root mean square deviation from the structure coordinates of the backbone atoms of the amino acids as set out in Table 7 of less than or equal to about 2.0 angstroms.

35. (New) The method of claim 3, wherein:

optimizing a helix bundle configuration includes calculating a minimum-energy configuration for the helix bundle in a lipid bilayer.

36. (New) The method of claim 1, wherein:

the membrane-bound protein is a G-protein coupled receptor.

37. (New) The method of claim 1, wherein:

identifying two or more ranges of amino acids in the amino acid sequence as transmembrane regions includes aligning the amino acid sequence with an experimental or theoretical helical template.

38. (New) The method of claim 1, wherein:

identifying two or more ranges of amino acids in the amino acid sequence as transmembrane regions includes determining the periodicity of hydrophobic residues in the amino acid sequence; and

optimizing a helix bundle configuration includes identifying a plurality of lipid-accessible residues based at least in part on the determined periodicity.

39. (New) The method of claim 1, wherein:

constructing each of two or more helices in a set of helices for the transmembrane regions includes optimizing each of the two or more helices in the set of helices using a torsional molecular dynamics method.

40. (New) The method of claim 39, wherein:

the torsional molecular dynamics method uses the Newton-Euler Inverse Mass Operator.

41. (New) The method of claim 1, wherein:

constructing each of two or more helices in a set of helices for the transmembrane regions includes determining 3-D coordinates that define the structure of each helix in the set of helices.

42. (New) The method of claim 1, wherein:

optimizing a helix bundle configuration includes determining a rotation and tilt of each helix in the set of helices.

43. (New) The method of claim 1, wherein:

optimizing a helix bundle configuration includes orienting the helix axes according to the 7.5 Å electron density map for rhodopsin.

44. (New) The method of claim 38, wherein:

optimizing a helix bundle configuration includes orienting the identified lipid-accessible residues to face the outside of the helix bundle.

45. (New) The method of claim 1, wherein:

the first molecular dynamics simulation is a rigid body molecular dynamics simulation.

46. (New) The method of claim 1, wherein:

optimizing a helix bundle configuration for the set of helices includes modeling the effect of the environment of the membrane-bound protein.

47. (New) The method of claim 45, wherein:

the first molecular dynamics simulation uses the DREIDING force field, charges simulating the membrane, and charges for the transmembrane protein.

48. (New) The method of claim 1, wherein:

the second molecular dynamics simulation is a mixed mode molecular dynamics simulation.

49. (New) The method of claim 48, wherein:

the second molecular dynamics simulation uses a torsional molecular dynamics method to model the helices and inter-helical loops and a rigid body molecular dynamics method to model the membrane of the transmembrane protein.

50. (New) The method of claim 1, wherein:

the second molecular dynamics simulation includes dynamic optimization of the structure using cell multipole methods or fast torsional dynamic methods.

51. (New) The method of claim 1, wherein:

at least the second molecular dynamics simulation includes a solvent approximation.

52. (New) The method of claim 51, wherein:

the solvent approximation is a continuum solvation model.

53. (New) The method of claim 52, wherein:

the solvent approximation includes the Surface Generalized Born model or the Poisson-Boltzmann description.

54. (New) The method of claim 53, wherein:

the solvent approximation is an empirical approximation comprising estimating solvation free energy as a function of solvent accessible protein surface area.

55. (New) The method of claim 1, wherein:

the predicted structure is generated by performing the second molecular dynamics simulation for a time in the range from about 100ps to about 1 ns.

56. (New) The method of claim 1, wherein:

the set of helices includes four or more helices.

57. (New) The method of claim 1, wherein:

the set of helices includes seven or more helices.